their heads. Hitherto, people have been taking the long view, planning to practice for a few years on nematodes, *Arabidopsis* and *Drosophila*, before turning their attention, and the techniques learned in the earlier stages, to the human genome. On that leisurely timetable, a nucleotide sequence of the human genome would be complete sometime in the first decade of the next century. Does Venter's gallop through the genome render the slower programmes redundant?

The simple truth, of course, is that it does not. Venter isolates only tags, represented by nucleotide sequences of variable length, from the ends of genes. Indeed, it is worse than that: the tags are DNA molecules complementary to the ends of RNA molecules recovered from the cytoplasm of a cell. While they may represent the genes active in particular tissues, they can say nothing about the parts of those genes which are not expressed (called introns) nor about the apparently meaningless DNA in which many genes are embedded (called 'junk', Crick's word). Even so, Venter's approach offers quick way of labelling active genes (whence the name 'tag') which can be located within the genome and then fished out from it so that their complete sequence can, if necessary, be determined. That is grist for the mills of those who want to understand the particular functions of particular genes, which is how medical practice will be eventually improved. So the more complicated truth about the complementary DNA (cDNA) technique is that it is a threat to the classical human genome projects; agencies will more readily fund the former than the latter.

That would be mistaken. Several important features of the human and any other genome might then indefinitely be mysteries. That there should be introns within genes has been a puzzle since they were first recognized in 1980. Are they functional, and if so how, or perhaps vestigial and, if so, with what meaning? Is the 'junk' really junk, and even so, may there be evolutionary lesson to be learned from the comparison of one creature's junk with another's? Then, since the human genome (or any other) contains not just a specification of the components of each cell but a recipe for making them, must not the detailed arrangement of the genome embody not merely the structure of all of an organism's molecules but the work-plan for generating them as and when required? And who would say that answers to such questions as these would be without medical benefit?

What this implies is that the two approaches to the structure of the human genome are neither in conflict nor complementary but different. The classical human genome project, figuratively (only) that of starting from one end and working through to the other 3 billion base-pairs later, will yield information that the cDNA technique cannot. To abandon the first because the second will yield immediately useful information would be like trying to teach a person a foreign language by instructing him only on the meanings of the nouns. The difficulty, at least until the dust has settled, is that the cDNA sequences, which would be of great value to the larger project, are likely to be generated most rapidly under the umbrellas of companies and may not be published until patent rights are granted , whenever that may be. That would be a great waste of effort. □

Vaccine compromise

The money about to be wasted on a clinical trial for AIDS vaccines could be better spent on basic science.

In what at first looked like a triumph of military might over common sense and sound scientific judgement, the US Army decided last week to go ahead with a $20 million trial of a "therapeutic" AIDS vaccine despite objections from the US National Institutes of Health (NIH) and the Food and Drug Administration (FDA) (see page 581). The vaccine, based on the gp160 subunit of the human immunodeficiency virus (HIV), is promoted by its manufacturer (a small Connecticut company called MicroGeneSys) as a significant new therapy for AIDS. The trial was mandated by Congress last year only after extensive lobbying by a company that has aggressively promoted its product.

But even as word of the Army's decision to proceed despite scientific opposition become known, NIH and FDA officials, as well as AIDS activists, were protesting to the White House and the Department of Defense that any trial should include several candidate therapeutic vaccines now being studied, not just the one from MicroGeneSys. Perhaps surprisingly, the NIH and FDA seem to have carried the day and their apparent success in demanding a multi-vaccine trial is seen as the virtuous triumph of science.

In a way it is. If the United States is going to spend $20 million or more to test these vaccines on thousands of patients, it is better to evaluate all candidate vaccines. The NIH feels so strongly about a multi-vaccine approach that would include patients from minority groups, intravenous drug users and others with AIDS who are not in the military that it has volunteered to add money to the pot, thereby taking the wind out of the Army's argument that a broad trial would cost more than the $20 million Congress has allocated.

But the real issue is whether any therapeutic vaccine should proceed. Taking the MicroGeneSys case as an example, the argument is that the gp160 subunit might lead to an immune stimulation sufficient to produce a clinically meaningful halt to HIV in people who are already infected. In this sense, the therapeutic vaccine is more like a drug than a traditional vaccine, which is meant to prevent infection in the first place. But the accumulation of new data, many of them dependent on refined techniques, such as PCR (polymerase chain reaction), for finding HIV in people who are infected but not yet afflicted with overt AIDS, suggests that, within weeks of infection, HIV in massive quantities has seeded the lymph nodes and is present in blood (see *Nature*, **362**, 355; 1993). A therapeutic vaccine may simply be too little too late. Certainly trials enrolling thousands of patients are not yet in order.

At this point, NIH, FDA, the Army and Congress should do the right thing and reevaluate the entire premise of this $20 million trial which, by implication, holds the promise of a significant advance in the treatment of AIDS. If they do not, they stand accused of playing politics with people suffering from a complex and still lethal disease. □